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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,968	09/19/2000	Ping Yip	24736-2049	4499

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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/663,968	YIP, PING	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-62,66-69,73 and 84-91* is/are rejected.

7)☒ Claim(s) *63-65,70-72,74 and 79-83* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 46-91 are pending.

Claims 1-45 are cancelled.

Claims 46-91 are being examined.

Applicants' arguments to the objections/rejections stated in the previous office action have been fully considered and are persuasive in part. Rejections not reiterated hereby withdrawn. The following rejections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 46, 66-69, 73, 77, 78, and 84-91 rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (US PAT 5, 853,979), in view of Dunkel (US PAT 5,572,125).

The claims are directed to an automated method, computerized system, system, and machine-readable program operating on a computer for identifying a component in a DNA sample using a mass spectrometer to generate a machine readable data set and

analyzing the data by generating denoised data by performing noise reduction, correcting a baseline for the denoised data to generate an intermediate data set, defining peaks in the intermediate data set, subtracting the peaks from the intermediate data set to generate a residual data set, removing the residual data set from the intermediate data set to produce a corrected data set, locating peaks in the corrected data set and identifying the component that corresponds to each located peak.

Green et al teach a method, a computerized system, system, and machine-readable program operating on a computer for identifying a component in a DNA sample using a mass spectrometer (col. 5, line 18 to generate a machine readable data set and analyzing the data by performing noise reduction to generate denoised data, correcting a baseline for the denoised experimental data representing an intermediate data set, defining peaks in the intermediate data set as "fragment pattern" (col. 5, lines 9-43). Green et al further teach the computer is integral to the instrument (cl. 85)(col 16, line 27-39).

Green et al do not teach the removal of peaks and subsequent generation and removal of a residual baseline from the denoised experimental data.

Dunkel et al teach method of automated analysis and correction of spectral data obtained through ion cyclotron mass spectrometry (col. 1, lines 16-19). Dunkel et al teach that the residual baseline obtained by removing peaks from experimental data can be applied to the experimental data to correct for baseline distortion (col. 11, lines 2-3). Dunkel teach the generation of a residual baseline by subtracting modeled peak data from the experimental "intermediate" data (cls. 67-69)(col. 20, lines 40-45) Dunkel

et al teaches identifying includes identifying peak probabilities for the putative peak and is derived using signal to noise ratio (cls. 77, 78, 88, 89, 90)(col.32, lines 27-29 and 48-51; and col. 33, lines 3 and 15-20). Dunkel et al teach the modeling of peaks by fitting a gaussian curve (cl. 73)(col. 8, lines 5-7). Dunkel et al teach performing a mass shift of the peak position (cl. 66)(col. 2, lines 43-46).

It would have been obvious to one of skill in the art to combine the method for correction of spectral data of Dunkel with the method intermediate data set generation of Green et al because Green et al teach that other signal processing techniques can be applied to generate clean, corrected data (col. 5, lines 47-49) and Dunkel teaches that baseline correction can be corrected by subtracting the residual baseline.

One would have been motivated to do so because Dunkel teaches that the residual baseline subtraction speeds up data analysis, improves the reliability of signal detection, and allows for the analysis of data sets of increased complexity (col. 33, lines 62-67).

2. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (US PAT 5, 853,979), in view of Dunkel (US PAT 5,572,125) as applied to claim 46 above, and further in view of Stanton et al (US PAT 6,440,705).

Claim 47 is directed to mass spectrometry that is MALDI-TOF.

Stanton et al teach DNA analysis by MALDI-TOF mass spectrometry (col.9, lines 15-31).

It would have been obvious to one of skill in the art to combine the application of MALDI-TOF analysis of DNA of Stanton et al with the method of mass spectrometry DNA spectral analysis of Green and the residual baseline generation of Dunkel et al because Stanton et al teach that MALDI-TOF is capable of ionizing DNA without further fragmentation (col. 9, line 22-23) whereas other mass spectrometry techniques can lead to further fragmentation (col. 16, line 60-62).

One would have been motivated with a reasonable expectation of success to do so because Stanton et al teach the fulfillment of the need for a simple low cost, rapid, yet sensitive and accurate method for analyzing polynucleotides (col. 13, lines 43-46).

3. Claims 48-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (US PAT 5, 853,979), in view of Dunkel (US PAT 5,572,125) as applied to claim 46 above, and further in view of Shew et al (US PAT 5,436,447).

The combination of references of Dunkel and Green et al do not teach noise reduction ("denoising") using wavelet technology transforms.

Shew et al teach utilizing wavelet technology transforms to reduce noise in mass spectrometry data. Shew et al teach the denoising includes the generation of a noise profile using wavelet technology in a series of stages or "transients" (cl. 48 and 49) (col. 7, lines 64-65). Shew et al teach generating a noise profile for stage 0 i.e. the mother wavelet (cl. 50)(col 3, lines 30-48). Shew et al also teach generating other noise profiles by applying a scale factor to the stage 0 noise profile (cl. 51 and 52)(col. 8, line 61 and col 3, lines 30-48). Shew et al teach applying a threshold ("desired level") to selected

stages and added to the noise profile where the threshold is scaled before being applied and the scaling factors are less at higher stages (cl. 53-56) (col. 8, lines 55-60, col. 11, lines 5-7 and col. 16, lines 1-3). Shew et al teach the generation of sparse data set (cl. 57)(col. 6, lines 19-26). Shew et al teach shifting the denoised data (cl. 58) (col. 16, lines 41-45).

It would have been obvious to combine the wavelet technology to reduce noise in spectral data of Shew et al with the method of mass spectrometry DNA spectral analysis of Green and the residual baseline generation of Dunkel et al because Shew et al teach wavelet technology transforms allow for more accurate determinations for the relative ion abundances in a mass spectrometry sample (abstract).

One would have had a reasonable expectation of success and been motivated to do so by Dunkel who teaches that the method allows to speed up data analysis, improves the reliability of signal detection, and allows for the analysis of data sets of increased complexity (col. 33, lines 62-67). One would have also been motivated by Green et al who teach increasing the speed of DNA sample analysis with improved accuracy (col. 3, line 17-20).

4. Claim 59-62 rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (US PAT 5, 853,979), in view of Dunkel (US PAT 5,572,125) as applied to claim 46 above, and further in view of Gavin et al (US PAT 6, 586, 728).

The combination of references of Dunkel and Green et al do not teach the generating a moving average of the denoised data as a further correction of the

baseline and identification of peaks. Green, however teaches that other signal processing techniques can be applied to generate clean, corrected data.

Gavin teaches the filtering of spectrometry data by application of a moving average filter to identify peak sections (col. 4, lines 8-25). Gaviin et al further demonstrate the application a moving average filter results in the smoothing of the spectral data and reduction of noise (figures 3-6).

It would have been obvious to combine the application of the moving average filter such as those described in Gavin et al to improve the quality of the intermediate data set generation of Green et al because Green et al teach that other signal processing techniques can be applied to generate clean, corrected data (col. 5, lines 47-49), and by Gavin et al who teach that the moving average filter optimizes the trade offs of increasing the signal to noise ratio and has the least negative effect on mass resolution (col. 3, line 19-24).

5. Claim 63-65, 70-72, 74 and 79-83 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conlcusion

No claims allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karlheinz R. Skowronek/

MICHAEL BORIN, PH.D
PRIMARY EXAMINER